CLAIMS

1. Use of a CB_1 receptor antagonist for the preparation of drugs useful in the treatment of appetency disorders.

2. Use according to claim 1 for the preparation of drugs intended for regulating consumption desires.

3. Use according to claim 1 for the preparation of drugs useful in the treatment of disorders associated with a substance.

4. Use according to claim 1 for the preparation of drugs useful in the treatment of disorders of food behaviors.

5. Use according to claim 1 for the preparation of drugs useful in the treatment of obesity.

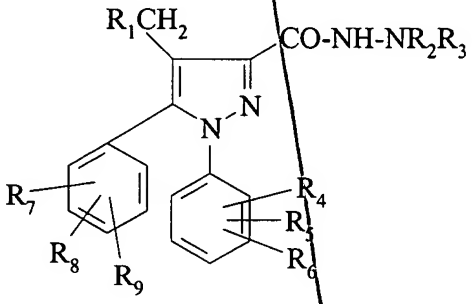
6. Use according to claim 5 for the preparation of drugs useful in the treatment of obesity associated with non-insulin-dependent diabetes.

7. Use according to claim 1 for the preparation of drugs useful in the treatment of any disease resulting in the patient becoming overweight.

8. Use according to claim 1 for the preparation of drugs useful in the treatment of bulimia.

9. Use according to claim 1 for the preparation of drugs useful in the treatment of drug abuse or drug dependency.

10. Use according to any one of claims 1 to 9, characterized in that the CB_1 receptor antagonist is a compound of the formula



(II)

in which:

- R_1 is hydrogen, a fluorine, a hydroxyl, a $(C_1\text{-}C_5)$alkoxy, a $(C_1\text{-}C_5)$alkylthio, a hydroxy$(C_1\text{-}C_5)$alkoxy, a group $-NR_{10}R_{11}$, a cyano, a $(C_1\text{-}C_5)$alkylsulfonyl or a $(C_1\text{-}C_5)$alkylsulfinyl;

- R_2 and R_3 are a $(C_1$-$C_4)$alkyl or, together with the nitrogen atom to which they are bonded, form a saturated or unsaturated 5- to 10-membered heterocyclic radical which is unsubstituted or monosubstituted or polysubstituted by a $(C_1$-$C_3)$alkyl or by a $(C_1$-$C_3)$alkoxy;
- R_4, R_5, R_6, R_7, R_8 and R_9 are each independently hydrogen, a halogen or a trifluoromethyl, and if R_1 is a fluorine, R_4, R_5, R_6, R_7, R_8 and/or R_9 can also be a fluoromethyl, with the proviso that at least one of the substituents R_4 or R_7 is other than hydrogen;
- R_{10} and R_{11} are each independently hydrogen or a $(C_1$-$C_5)$alkyl, or R_{10} and R_{11}, together with the nitrogen atom to which they are bonded, form a heterocyclic radical selected from pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl and piperazin-1-yl, which is unsubstituted or substituted by a $(C_1$-$C_4)$alkyl,

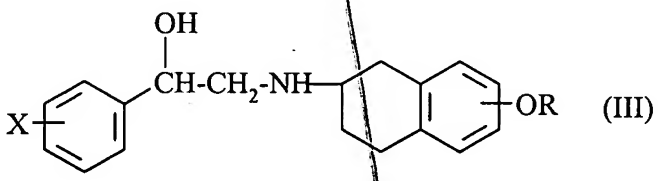
one of its salts or one of their solvates.

11. Use according to claim 10, characterized in that the CB_1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates.

12. Use according to any one of claims 1 to 8, 10 or 11, characterized in that the CB_1 receptor antagonist is associated with a regulator of metabolic disorders.

13. Use according to claim 12, characterized in that said regulator of metabolic disorders is a β_3-agonist.

14. Use according to claim 13, characterized in that said β_3-agonist is a compound of the formula



(III)

in which:

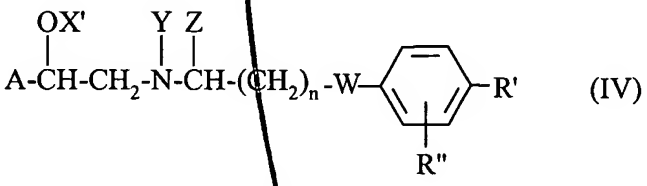
- X is hydrogen, a halogen, a trifluoromethyl or a $(C_1$-$C_4)$alkyl; and
- R is hydrogen or a methyl which is unsubstituted or substituted by a carboxyl or an alkoxycarbonyl in which the alkoxy is $(C_1$-$C_6)$,

or one of its pharmaceutically acceptable salts.

15. Use according to claim 14, characterized in that said β_3-agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-

chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

16. Use according to claim 13, characterized in that said β_3-agonist is a compound of the formula



(IV)

in which:

- n is 1, 2 or 3;
- A is a benzofuran-2-yl or a phenyl which is unsubstituted or substituted by one or two halogen atoms or by a $(C_1\text{-}C_4)$alkyl or a trifluoromethyl;
- R′ is:
  - hydrogen;
  - a $(C_1\text{-}C_6)$alkyl;
  - a functional group selected from the following groups: hydroxyl; $(C_1\text{-}C_6)$-alkoxy; $(C_2\text{-}C_6)$alkenyloxy; $(C_2\text{-}C_6)$alkynyloxy; $(C_3\text{-}C_8)$cycloalkoxy; $(C_3\text{-}C_8)$cycloalkyl$(C_1\text{-}C_6)$alkoxy; benzyloxy; phenoxy; mercapto; $(C_1\text{-}C_6)$alkylthio; $(C_2\text{-}C_6)$alkenylthio; $(C_2\text{-}C_6)$alkynylthio; $(C_3\text{-}C_8)$cycloalkylthio; $(C_3\text{-}C_8)$cycloalkyl$(C_1\text{-}C_6)$alkylthio; benzylthio; phenylthio; $(C_1\text{-}C_6)$alkylsulfinyl; $(C_2\text{-}C_6)$alkenylsulfinyl; $(C_2\text{-}C_6)$alkynylsulfinyl; $(C_3\text{-}C_8)$cycloalkylsulfinyl; $(C_3\text{-}C_8)$cycloalkyl$(C_1\text{-}C_6)$alkylsulfinyl; benzylsulfinyl; phenylsulfinyl; $(C_1\text{-}C_6)$alkylsulfonyl; $(C_2\text{-}C_6)$alkenylsulfonyl; $(C_2\text{-}C_6)$alkynylsulfonyl; $(C_3\text{-}C_8)$cycloalkylsulfonyl; $(C_3\text{-}C_8)$cycloalkyl$(C_1\text{-}C_6)$alkylsulfonyl; benzylsulfonyl; phenylsulfonyl; cyano; nitro; amino which is unsubstituted or substituted by one or two identical or different radicals selected from $(C_1\text{-}C_6)$alkyl, $(C_2\text{-}C_6)$alkenyl, $(C_2\text{-}C_6)$alkynyl, $(C_3\text{-}C_8)$cycloalkyl, $(C_3\text{-}C_8)$cycloalkyl$(C_1\text{-}C_6)$alkyl, benzyl and phenyl groups; carboxyl; alkoxycarbonyl in which the alkoxy is $(C_1\text{-}C_6)$; $(C_2\text{-}C_6)$-alkenyloxycarbonyl; $(C_2\text{-}C_6)$alkynyloxycarbonyl; $(C_3\text{-}C_8)$cycloalkoxycarbonyl; $(C_3\text{-}C_8)$cycloalkyl$(C_1\text{-}C_6)$alkoxycarbonyl; benzyloxycarbonyl; phenoxycarbonyl; or carbamoyl which is unsubstituted or substituted on the amino group by one or two identical or different radicals

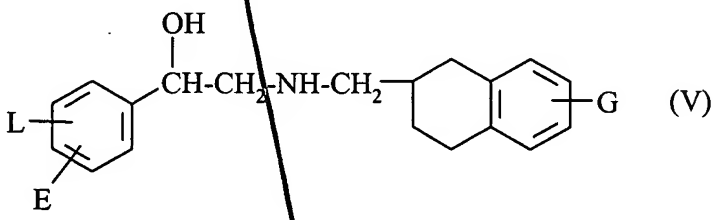
selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_8)-cycloalkyl, (C_3-C_8)cycloalkyl(C_1-C_6)alkyl, benzyl and phenyl groups;

- a group R''' selected from the following groups: (C_1-C_6)alkyl substituted by a functional group; (C_2-C_6)alkenyl substituted by a functional group; (C_2-C_6)-alkynyl substituted by a functional group; phenyl(C_1-C_6)alkyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; phenyl(C_2-C_6)alkenyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; phenyl(C_2-C_6)alkynyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; benzyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; and phenyl which is unsubstituted or substituted by a (C_1-C_6)alkyl or by a functional group, the functional group being as defined above;
- a group O-R''', S-R''', SO-R''' or SO_2-R''', in which R''' is as defined above;
- a group NR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group COOR''' or a group CO-SR''', in which R''' is as defined above;
- a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group SO_2NR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- R'' is hydrogen; a halogen; a (C_1-C_6)alkyl; a functional group as defined above; a group OR''', R''' being as defined above; a group COOR''', R''' being as defined above; or a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- W is a direct bond or an oxygen atom;
- X' is hydrogen, a (C_1-C_6)alkyl or a (C_1-C_6)alkylcarbonyl;
- Y is hydrogen or a group A'-CH(OH)-CH_2-, A' being identical to A but other than benzofuran-2-yl; or

- X′ and Y, taken together, form a methylene group optionally substituted by an alkoxycarbonyl in which the alkoxy is (C_1-C_6); an ethylene group optionally substituted by an oxo group; or a 1,3-propylene group;
- Z is hydrogen or a (C_1-C_6)alkyl,

or one of its pharmaceutically acceptable salts.

17. Use according to claim 13, characterized in that said β_3-agonist is a compound of the formula



(V)

in which:

- E is hydrogen, a (C_1-C_4)alkyl, a (C_1-C_4)alkoxy, a phenyl, a nitro, a halogen atom or a trifluoromethyl;
- L is hydrogen, a (C_1-C_4)alkyl, a (C_1-C_4)alkoxy, a phenyl, a nitro or a halogen atom; or E and L together are a group -CH=CH-CH=CH- or -CH_2-CH_2-CH_2-CH_2-; and
- G is hydrogen, a chlorine atom, a hydroxyl or a group OG′, in which G′ is a (C_1-C_4)alkyl which is unsubstituted or substituted by a hydroxyl, (C_1-C_4)alkoxy, (C_1-C_4)alkoxycarbonyl, carboxyl or (C_3-C_7)cycloalkyl; a (C_3-C_7)cycloalkyl; or a (C_2-C_4)alkanoyl,

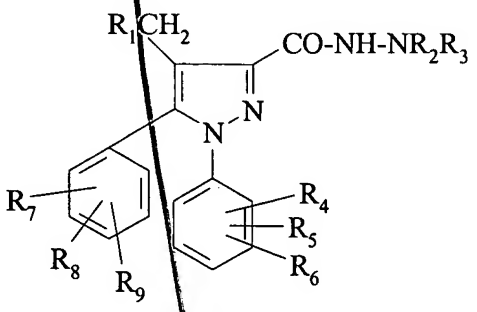
or one of its pharmaceutically acceptable salts.

18. Use according to claim 13, characterized in that the CB_1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates and the β_3-agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

19. A pharmaceutical composition containing a CB_1 receptor antagonist and a regulator of metabolic functions with a pharmaceutical excipient.

20. A pharmaceutical composition according to claim 19, characterized in that said regulator of metabolic functions is a β_3-agonist.

21. A pharmaceutical composition according to claim 19 or 20, characterized in that the CB_1 receptor antagonist is a compound of the formula



(II)

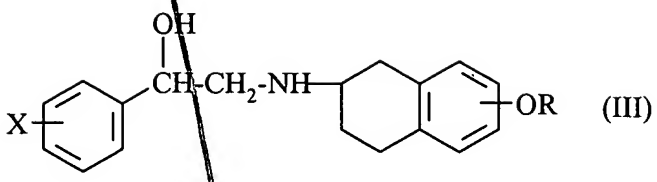
in which:

- R_1 is hydrogen, a fluorine, a hydroxyl, a $(C_1$-$C_5)$alkoxy, a $(C_1$-$C_5)$alkylthio, a hydroxy$(C_1$-$C_5)$alkoxy, a group $-NR_{10}R_{11}$, a cyano, a $(C_1$-$C_5)$alkylsulfonyl or a $(C_1$-$C_5)$alkylsulfinyl;
- R_2 and R_3 are a $(C_1$-$C_4)$alkyl or, together with the nitrogen atom to which they are bonded, form a saturated or unsaturated 5- to 10-membered heterocyclic radical which is unsubstituted or monosubstituted or polysubstituted by a $(C_1$-$C_3)$alkyl or by a $(C_1$-$C_3)$alkoxy;
- R_4, R_5, R_6, R_7, R_8 and R_9 are each independently hydrogen, a halogen or a trifluoromethyl, and if R_1 is a fluorine, R_4, R_5, R_6, R_7, R_8 and/or R_9 can also be a fluoromethyl, with the proviso that at least one of the substituents R_4 or R_7 is other than hydrogen;
- R_{10} and R_{11} are each independently hydrogen or a $(C_1$-$C_5)$alkyl, or R_{10} and R_{11}, together with the nitrogen atom to which they are bonded, form a heterocyclic radical selected from pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl and piperazin-1-yl, which is unsubstituted or substituted by a $(C_1$-$C_4)$alkyl,

one of its salts or one of their solvates.

22. A pharmaceutical composition according to claim 21, characterized in that the CB_1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates.

23. A pharmaceutical composition according to any one of claims 20 to 22, characterized in that the β_3-agonist is a compound of the formula



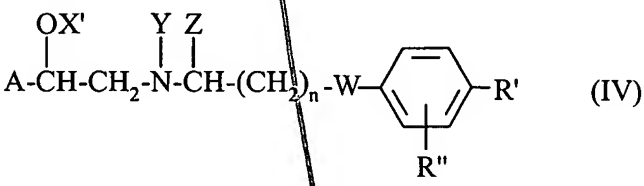
(III)

in which:

- X is hydrogen, a halogen, a trifluoromethyl or a (C_1-C_4)alkyl;
- R is hydrogen or a methyl which is unsubstituted or substituted by a carboxyl or an alkoxycarbonyl in which the alkoxy is (C_1-C_6),

or one of its pharmaceutically acceptable salts.

24. A pharmaceutical composition according to any one of claims 20 to 22, characterized in that the β_3-agonist is a compound of the formula



(IV)

in which:

- n is 1, 2 or 3;
- A is a benzofuran-2-yl or a phenyl which is unsubstituted or substituted by one or two halogen atoms or by a (C_1-C_4)alkyl or a trifluoromethyl;
- R′ is:
  - hydrogen;
  - a (C_1-C_6)alkyl;
  - a functional group selected from the following groups: hydroxyl; (C_1-C_6)alkoxy; (C_2-C_6)alkenyloxy; (C_2-C_6)alkynyloxy; (C_3-C_8)cycloalkoxy; (C_3-C_8)-cycloalkyl(C_1-C_6)alkoxy; benzyloxy; phenoxy; mercapto; (C_1-C_6)alkylthio; (C_2-C_6)alkenylthio; (C_2-C_6)alkynylthio; (C_3-C_8)cycloalkylthio; (C_3-C_8)-cycloalkyl(C_1-C_6)alkylthio; benzylthio; phenylthio; (C_1-C_6)alkylsulfinyl; (C_2-C_6)alkenylsulfinyl; (C_2-C_6)alkynylsulfinyl; (C_3-C_8)cycloalkylsulfinyl; (C_3-C_8)-cycloalkyl(C_1-C_6)alkylsulfinyl; benzylsulfinyl; phenylsulfinyl; (C_1-C_6)alkyl-sulfonyl; (C_2-C_6)alkenylsulfonyl; (C_2-C_6)alkynylsulfonyl; (C_3-C_8)cycloalkyl-sulfonyl; (C_3-C_8)cycloalkyl(C_1-C_6)alkylsulfonyl; benzylsulfonyl;

phenylsulfonyl; cyano; nitro; amino which is unsubstituted or substituted by one or two identical or different radicals selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_8)cycloalkyl, (C_3-C_8)cycloalkyl(C_1-C_6)alkyl, benzyl and phenyl groups; carboxyl; alkoxycarbonyl in which the alkoxy is (C_1-C_6); (C_2-C_6)alkenyloxycarbonyl; (C_2-C_6)alkynyloxycarbonyl; (C_3-C_8)cycloalkoxycarbonyl; (C_3-C_8)cycloalkyl(C_1-C_6)alkoxycarbonyl; benzyloxycarbonyl; phenoxycarbonyl; and carbamoyl which is unsubstituted or substituted on the amino group by one or two identical or different radicals selected from (C_1-C_6)alkyl, (C_2-C_6)alkenyl, (C_2-C_6)alkynyl, (C_3-C_8)-cycloalkyl, (C_3-C_8)cycloalkyl(C_1-C_6)alkyl, benzyl and phenyl groups;

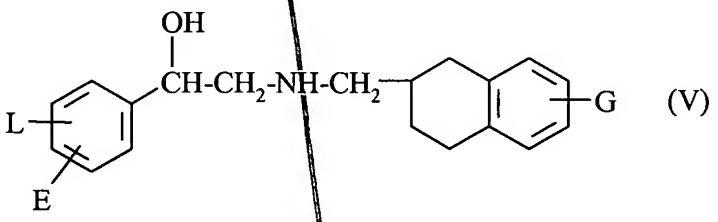
- a group R‴ selected from the following groups: (C_1-C_6)alkyl substituted by a functional group; (C_2-C_6)alkenyl substituted by a functional group; (C_2-C_6)-alkynyl substituted by a functional group; phenyl(C_1-C_6)alkyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; phenyl(C_2-C_6)alkenyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; phenyl(C_2-C_6)alkynyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; benzyl substituted on the phenyl by a (C_1-C_6)alkyl or by a functional group; and phenyl which is unsubstituted or substituted by a (C_1-C_6)alkyl or by a functional group, the functional group being as defined above;
- a group O-R‴, S-R‴, SO-R‴ or SO_2-R‴, in which R‴ is as defined above;
- a group NR‴R°, in which R‴ is as defined above and R° is hydrogen or is as defined above for R‴, or R‴ and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group COOR‴ or a group CO-SR‴, in which R‴ is as defined above;
- a group CONR‴R°, in which R‴ is as defined above and R° is hydrogen or is as defined above for R‴, or R‴ and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- a group SO_2NR‴R°, in which R‴ is as defined above and R° is hydrogen or is as defined above for R‴, or R‴ and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;
- R″ is hydrogen; a halogen; a (C_1-C_6)alkyl; a functional group as defined above; a group OR‴, R‴ being as defined above; a group COOR‴, R‴ being as defined

above; or a group CONR'''R°, in which R''' is as defined above and R° is hydrogen or is as defined above for R''', or R''' and R°, together with the nitrogen to which they are bonded, form a group selected from pyrrolidino, piperidino and morpholino groups;

- W is a direct bond or an oxygen atom;
- X' is hydrogen, a (C_1-C_6)alkyl or a (C_1-C_6)alkylcarbonyl;
- Y is hydrogen or a group A'-CH(OH)-CH_2-, A' being identical to A but other than benzofuran-2-yl; or
- X' and Y, taken together, form a methylene group optionally substituted by an alkoxycarbonyl in which the alkoxy is (C_1-C_6); an ethylene group optionally substituted by an oxo group; or a 1,3-propylene group;
- Z is hydrogen or a (C_1-C_6)alkyl,

or one of its pharmaceutically acceptable salts.

25. A pharmaceutical composition according to any one of claims 20 to 22 wherein the β_3-agonist is a compound of the formula



(V)

in which:

- E is hydrogen, a (C_1-C_4)alkyl, a (C_1-C_4)alkoxy, a phenyl, a nitro, a halogen atom or a trifluoromethyl;
- L is hydrogen, a (C_1-C_4)alkyl, a (C_1-C_4)alkoxy, a phenyl, a nitro or a halogen atom; or E and L together are a group -CH=CH-CH=CH- or -CH_2-CH_2-CH_2-CH_2-; and
- G is hydrogen, a chlorine atom, a hydroxyl or a group OG', in which G' is a (C_1-C_4)alkyl which is unsubstituted or substituted by a hydroxyl, (C_1-C_4)alkoxy, (C_1-C_4)alkoxycarbonyl, carboxyl or (C_3-C_7)cycloalkyl; a (C_3-C_7)cycloalkyl; or a (C_2-C_4)alkanoyl,

or one of its pharmaceutically acceptable salts.

26. A pharmaceutical composition according to claim 23, characterized in that the β_3 agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-

(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

27. A pharmaceutical composition according to any one of claims 20 to 26 containing from 0.5 to 600 mg of CB_1 receptor antagonist and from 0.5 to 600 mg of β_3-agonist.

28. A pharmaceutical composition according to claim 27 containing from 1 to 400 mg of CB_1 receptor antagonist and from 2 to 400 mg of β_3-agonist.

29. A pharmaceutical composition according to claim 28 containing from 2 to 200 mg of CB_1 receptor antagonist and from 10 to 250 mg of β_3-agonist.

30. A kit for the treatment of appetency disorders, which contains:
- a CB_1 receptor antagonist, and
- a regulator of metabolic disorders,
said active principles being in separate compartments and being intended to be administered simultaneously, sequentially or over a period of time.

31. A kit according to claim 30 in which said regulator of metabolic disorders is a β_3-agonist.

32. A kit according to claim 30 or 31 in which said CB_1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates and said β_3-agonist is N-[(2S)-7-ethoxycarbonylmethoxy-1,2,3,4-tetrahydronaphth-2-yl]-(2R)-2-(3-chlorophenyl)-2-hydroxyethanamine or one of its pharmaceutically acceptable salts.

33. A kit according to any one of claims 30 to 32 in which said active principles are in different packagings.

34. Use according to claim 1 for the preparation of a drug useful for regulating the desire to consume non-essential food items.

35. Use according to claim 34 in which the non-essential food items are excess sugars, excess carbohydrates, alcohol and drugs.

36. Use of a CB_1 receptor antagonist for the preparation of a drug useful to suppress spontaneous appetency for a food item which usually brings pleasure.

37. Use according to claim 36 in which the food item found pleasurable is alcohol or sugar.

38. Use according to any one of claims 34 to 37 in which the CB_1 receptor antagonist is N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methylpyrazole-3-carboxamide, one of its pharmaceutically acceptable salts or one of their solvates.

add a4